Susceptibility Testing of Oritavancin against Vancomycin Resistant, Daptomycin non-Susceptible Enterococcus faecium Utilizing Commercially Available Gram-Positive Plates

Paskovtzy A PharmD  BCPS  AQ-ID, Shamis R.  Babady NE PhD, Kamboj M. MD*  See SK MD**
Memorial Sloan Kettering Cancer Center, New York, NY: Thomas Jefferson College of Pharmacy Philadelphia, PA

INTRODUCTION

Vancomycin-resistant enterococcal faecium (VRE) is a leading pathogen and a major therapeutic hurdle in immunocompromized patients, particularly those receiving hematopoietic stem cell transplantation (HSCT). VRE bacteremia in transplant recipients have been associated with mortality rates of 9-22%.1,2

New drugs have been approved for treatment of VRE. Daptomycin has been used "off label" for the treatment or salvage therapy for VRE infections including bacteremias. In addition to lack of coverage and efficacy, emergence of non-susceptible isolates has been reported.3-6 Mechanisms for daptomycin resistance have not been fully explained, although several genetic pathways have been described.7 In a 2011 report by Kamboj et al., daptomycin-resistant VRE bacteremia at Memorial Sloan Kettering Cancer Center (MSKCC) increased from 3.4% in 2007 to 15.2% in 2009.8 Among 78 patients with VRE bacteremia at MSKCC between Jan 1, 2012 - Dec 31, 2013, 53(68%) had an initial isolate with daptomycin MIC ≥ 4 mcg/mL.

Oritavancin is a semi-synthetic lipoglycopeptide that has been FDA-approved for "off label" for the treatment or salvage therapy for VRE infections including bacteremias.9-10 Oritavancin has shown activity against VRE with median MIC 0.06 mcg/mL. Oritavancin is a semisynthetic lipoglycopeptide that has been FDA-approved for "off label" use in the treatment or salvage therapy for VRE infections including bacteremias.11  However, breakpoints for dalbavancin, range: <0.5 mcg/mL; erythromycin range: <0.25 mcg/mL; fosfomycin range: <16 mcg/mL; oxacillin range: <4 mcg/mL; telavancin range: <0.03 mcg/mL; teicoplanin range: ≤1 mcg/mL; and vancomycin range: <4 mcg/mL.

Susceptibility Testing of Oritavancin against Vancomycin Resistant, Daptomycin non-Susceptible Enterococcus faecium

The study objective is to test Susceptibility Testing of Oritavancin against Vancomycin Resistant, Daptomycin non-Susceptible Enterococcus faecium with median MIC 0.06 mcg/mL. Nearly all (60/61, 98%) isolates had ceftaroline MIC > 8 mcg/mL. Susceptibility Testing of Oritavancin against Vancomycin Resistant, Daptomycin non-Susceptible Enterococcus faecium with median MIC 0.06 mcg/mL.

RESULTS (Cont.)

Table 1. Oritavancin MIC (mcg/mL) distributions and frequency (%) against Linezolid MIC (mcg/mL). Telavancin, Dalbavancin and Oritavancin MIC(mcg/mL)

<table>
<thead>
<tr>
<th>MIC ≤ 0.5 mcg/mL</th>
<th>0.06</th>
<th>0.12</th>
<th>0.25</th>
<th>0.50</th>
<th>1 mcg/mL</th>
<th>2 mcg/mL</th>
<th>4 mcg/mL</th>
<th>8 mcg/mL</th>
<th>16 mcg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linezolid MIC= 0.03 mcg/mL</td>
<td>49</td>
<td>31%</td>
<td>31%</td>
<td>24%</td>
<td>8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid MIC= 0.12 mcg/mL</td>
<td>57</td>
<td>38%</td>
<td>31%</td>
<td>24%</td>
<td>8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid MIC= 0.25 mcg/mL</td>
<td>49</td>
<td>31%</td>
<td>31%</td>
<td>24%</td>
<td>8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid MIC= 0.50 mcg/mL</td>
<td>57</td>
<td>38%</td>
<td>31%</td>
<td>24%</td>
<td>8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telavancin MIC= ≤ 0.5 mcg/mL</td>
<td>6</td>
<td>83%</td>
<td>17%</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telavancin MIC= 0.015 mcg/mL</td>
<td>6</td>
<td>83%</td>
<td>17%</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telavancin MIC= 0.03 mcg/mL</td>
<td>3</td>
<td>67%</td>
<td>33%</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telavancin MIC= 0.5 mcg/mL</td>
<td>3</td>
<td>67%</td>
<td>33%</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telavancin MIC= ≤ 1 mcg/mL</td>
<td>6</td>
<td>67%</td>
<td>33%</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telavancin MIC= &gt; 1 mcg/mL</td>
<td>6</td>
<td>67%</td>
<td>33%</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### RESULTS

Sixty-one isolates of vancomycin-resistant Enterococcus faecium with daptomycin MIC ≥ 4 mcg/mL were identified, with the remaining isolates tested had MICs of 4.0 mcg/mL. Each isolate represents unique patient bacteremia episode. Baseline clinical data is listed in Table 2.

Inoculum concentration for each isolate was within CLSI broth microdilution method guidelines

Oritavancin exhibited activity against VRE with median MIC 0.06 mcg/mL (range: 0.06-0.25 mcg/mL) (Figure 1). Sixty-one isolates with daptomycin MIC ≥ 4 mcg/mL, were tested against vancomycin-susceptible enterococci (vancomycin-susceptible isolates).4

Sixty-one isolates of vancomycin-resistant Enterococcus faecium with daptomycin MIC ≥ 4 mcg/mL, were tested against vancomycin-susceptible enterococci (vancomycin-susceptible isolates).4

DISCLOSURES

This study was funded by a research grant from the Medicines Company.

REFERENCES


